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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/673,738	09/29/2003	S. Edward Lee	PC23050A	1929
23913	7590	10/27/2006	EXAMINER	
			GRASER, JENNIFER E	
		ART UNIT		PAPER NUMBER
				1645

DATE MAILED: 10/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/673,738	LEE ET AL.	
	Examiner	Art Unit	
	Jennifer E. Graser	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 13 October 2006.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-15 is/are pending in the application.
 - 4a) Of the above claim(s) 13 and 15 is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1-12 and 14 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)	4) <input type="checkbox"/> Interview Summary (PTO-413)
2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)	Paper No(s)/Mail Date. _____.
3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)	5) <input type="checkbox"/> Notice of Informal Patent Application
Paper No(s)/Mail Date <u>12/29/03</u>	6) <input type="checkbox"/> Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group I, claims 1-12 and 14, in the reply filed on 10/13/06 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 13 and 15 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Claim Rejections - 35 USC § 112-second paragraph

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-12 and 14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-12 and 14 are vague and indefinite because it the mere recitation of a name, i.e., human sequence antibody, to describe the invention is not sufficient to satisfy the Statute's requirement of adequately describing and setting forth the inventive concept. Further, the name "human sequence antibody" is used for a multitude of different antibodies with very different structures. The metes and bounds of the claimed invention cannot be understood. The claim should provide any structural properties, such as the amino acid sequence of the protein the antibody binds or the deposit

information which represents the antibody or hybridoma, which would allow for one to identify the protein without ambiguity. The mere recitation of a name does not adequately define the claimed antibody. See also 112, first paragraph enablement rejection below.

Claim 5 is vague and indefinite because it is unclear what is encompassed by the phrase "identifying characteristics". The metes and bounds of the invention cannot be understood. What characteristics are being referred to?

Claim 6 is vague and indefinite due to the phrase "the hybridoma derived from the hybridoma deposited at a[s] ATCC deposit number PTS-4527". The term "derived" does not provide the character or properties from the source that are to be retained in the final product, e.g., paper is derived from wood but is very different from wood.

Claim 12 should recite that the antibody is "isolated" since the claim currently reads on the antibody residing in culture which does not appear to be Applicant's intention.

Claim 14 recites the limitation "an anti-CTLA4 antibody of claim 8 or 12. There is insufficient antecedent basis for this limitation in the claim because claims 8 or 12 (and the claims from which they depend, i.e., claim 11 and 1, do not recite an anti-CTLA4 antibody. They only recite a "human sequence antibody".

Claim Rejections - 35 USC § 112-Deposit

4. Claims 5 and 6 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to

which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification lacks complete deposit information for hybridoma ATCC deposit number PTA-4527. Because it is not clear that the properties of this hybridoma are known and publicly available or can be reproducibly isolated from nature without undue experimentation and because the best mode disclosed by the specification requires the use of the hybridoma, a suitable deposit for patent purposes is required.

If the deposit has been made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicant or assignees or a statement by an attorney of record who has authority and control over the conditions of the deposit over his or her signature and registration number stating that the deposit has been accepted by an International Depository Authority under the provisions of the Budapest Treaty, that all restrictions upon public access to the deposit will be replaced if viable samples cannot be dispensed by the depository is required. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State. Amendment of the specification to recite the date of the deposit and the complete name and full street address of the depository is required.

If the deposits have not been made under the provisions of the Budapest Treaty, then in order to certify that the deposits comply with the criteria set forth in 37 CFR §1.801-1.809, assurances regarding availability and permanency of deposits are required. Such assurance may be in the form of an affidavit or declaration by applicants

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or assignees or in the form of a statement by an attorney of record who has the authority and control over the conditions of deposit over his or her signature and registration number averring:

- (a) during the pendency of this application, access to the deposits will be afforded to the Commissioner upon request;
- (b) all restrictions upon the availability to the public of the deposited biological material will be irrevocably removed upon the granting of a patent on this application;
- (c) the deposits will be maintained in a public depository for a period of at least thirty years from the date of the deposit or for the enforceable life of the patent or for a period of five years after the date of the most recent request for the furnishing of a sample of the deposited biological material, whichever is longest; and
- (d) the deposits will be replaced if they should become non-viable or non-replicable.

In addition, a deposit of the biological material that is capable of self-replication either directly or indirectly must be viable at the time of the deposit and during the term of deposit. Viability may be tested by the depository. The test must conclude only that the deposited material is capable of reproduction. A viability statement for each deposit of a biological material not made under the Budapest Treaty must be filed in the application and must contain:

- 1)The name and address of the depository;
- 2)The name and address of the depositor;
- 3)The date of deposit;
- 4)The identity of the deposit and the accession number given by the depository;
- 5)The date of the viability test;
- 6)The procedures used to obtain a sample if the test is not done by the depository; and
- 7)A statement that the deposit is capable of reproduction.

As a possible means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

If the deposit was made after the effective filing date of the application for patent in the United States, a verified statement is required from a person in a position to corroborate that the cell line described in the specification as filed is the same as that deposited in the depository. Corroboration may take the form of a showing of a chain of custody from applicant to the depository coupled with corroboration that the deposit is identical to the biological material described in the specification and in the applicant's possession at the time the application was filed.

Applicant's attention is directed to In re Lundak, 773 F.2d. 1216, 227 USPQ 90 (CAFC 1985) and 37 CFR §1.801-1.809 for further information concerning deposit practice.

Claim Rejections - 35 USC § 112-Scope of Enablement

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-12 and 14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for "A hybridoma deposited as ATCC deposit number PTA-4537"; and "An isolated antibody produced from the hybridoma deposited as ATCC deposit number PTA-4537", does not reasonably provide enablement for "**Any** hybridoma which produces at least 200/300/390mg/ml of a human sequence antibody when cultured in batch culture"; "**any** hybridoma which produces at least 200/300/390mg/ml of a human sequence antibody when cultured in batch culture which is an anti-CTLA4 antibody"; "any hybridoma derived from or having the identifying characteristics of the hybridoma deposited as ATCC deposit number PTA-4537"; or for "a pharmaceutical composition for the treatment of cancer in a mammal comprising an amount of an anti-CTLA-4 antibody". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The instant specification recites that the invention is drawn to the development of hybridoma cell lines of human sequence monoclonal antibodies where the cell lines are adapted to grow in media lacking serum and other animal-derived components. It is

taught that animal cell culture typically have low production rates compared with bacterial cultures. It is taught that CTLA4 is involved in T-cell activation and that given the roles for CTLA4 in modulating T cell activation, uses for Mabs that have an affinity for CTLA4 are numerous. Anti-CTLA4 Mabs were known in the prior art.

The instant specification only provides description for a single hybridoma which produces a high production of anti-CTLA4 mAb, the hybridoma deposited with the ATCC as PTA-4537. The specification is silent to the production of any other human sequence antibody. According to prior art references, monoclonal antibodies can be readily produced; however, the total characterization of a monoclonal antibody is a long and complex procedure which varies widely with the intended use of the antibody. A general point is that if a single hybridoma has been produced and is intended for a specific function it is unlikely that the antibody produced will have all the required characteristics (Campbell, Laboratory Techniques, Vol. 13, pages 186-187, 1984). Campbell teaches that it is a waste of both reagents and time to attempt full characterization of an antibody which is not obtained from a fully cloned cell line. See Chapter 10, specifically page 186. Reproduction of an identical cell line and antibody is an extremely unpredictable event (see Campbell above). It does not appear that the claimed antibodies/hybridomas are known and publicly available or can be reproducibly isolated from nature without undue experimentation. Genentech Inc. v. Novo Nordisk A/S (CAFC) 42 USPQ2d 1001 clearly states: "Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. See Brenner v. Manson, 383 U.S. 519, 536, 148 USPQ

689, 696 (1966) (stating, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.") Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention." Additionally, the specification provides no examples that any of the antibodies recited in the instant specification, including the deposited antibody, could treat cancer in a mammal. The treatment of cancer is an extremely unpredictable error and absent any results or teachings, the specification does not enable this use. It is unpredictable that *any* hybridoma which produces *any* human sequence antibody in the claimed amounts could be produced without undue experimentation. The claims should be limited to the Deposited hybridoma and the Deposit requirements must be met (see Deposit rejection above).

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

8. Claims 1–12 and 14 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Hanson et al (WO 00/37504).

Hanson et al teach hybridomas which produce human sequence monoclonal antibodies, particularly anti-CTLA4 monoclonal antibodies. See pages 35-41. It is taught that a variety of different cell lines, either mammalian or non-mammalian, may be used to produce said antibodies depending on the level of expression required. particularly an antibody to CTLA4) could be produced in a Bacteria, yeast, insect and plant cell lines may be used for expression, as well as CHO, BHK, COS, Hep G2, etc..

See page 49. Accordingly, the levels recited in claims 1-11 would be encompassed by the teachings of Hanson, absent evidence to the contrary. If such is not found to be the case, then it would have been *prima facie* obvious to one of ordinary skill in the art that known monoclonal antibodies, e.g., any human sequence antibody (more specifically a CTLA4 antibody) could be produced in non-mammalian cell lines, such as a bacterial cell line, in order to increase production/yield of the antibodies because it was well known in the prior art at the time the invention was made that animal cell culture typically have low production rates compared with bacterial cultures. See Applicant's Admissions on page 1, lines 15-18, of the specification. Additionally, an antibody produced from the method of claim 11 would be expected to be identical to the claimed antibodies since it is also an anti-CTLA4 mAB. "The patentability of a product does not depend upon its method of production. If the product in [a] product-by-process claim is the same as or obvious from a product of the prior art, [then] the claim is unpatentable even though the prior [art] product was made by a different process." *In re Thorpe*, 227

USPQ 964, 966 (Fed. Cir. 1985) (citations omitted). Once the examiner provides a rationale tending to show that the claimed product appears to be the same or similar to that of the prior art, although produced by a different process, the burden shifts to applicant to come forward with evidence establishing an unobvious difference between the claimed product and the prior art product. *In re Marosi*, 218 USPQ 289, 292 (Fed. Cir. 1983). In product-by-process claims, “once a product appearing to be substantially identical is found and a 35 U.S.C. 102/103 rejection [is] made, the burden shifts to the applicant to show an unobvious difference.” MPEP 2113. This rejection under 35 U.S.C. 102/103 is proper because the “patentability of a product does not depend on its method of production.” *In re Thorpe*, 227 USPQ 964, 966 (Fed. Cir. 1985). The term “pharmaceutical composition for the treatment of cancer” (claim 14) is an intended use only. A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. A “pharmaceutically acceptable carrier” reads on water and therefore would be inherent in the preparation of the monoclonal antibodies.

9. Claims –12 and 14 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Korman et al (US 6,984,720). Hanson et al teach hybridomas which produce human sequence monoclonal antibodies, particularly anti-CTLA4 monoclonal antibodies. See columns 7-9 and 14.

Columns 24-33 teach that a variety of different cell lines, either mammalian or non-mammalian, may be used to produce said antibodies depending on the level of expression required. Accordingly, the levels recited in claims 1-11 would be encompassed by the teachings of Korman, absent evidence to the contrary. If such is not found to be the case, then it would have been *prima facie* obvious to one of ordinary skill in the art that known monoclonal antibodies, e.g., any human sequence antibody (more specifically a CTLA4 antibody) could be produced in non-mammalian cell lines, such as a bacterial cell line, in order to increase production/yield of the antibodies because it was well known in the prior art at the time the invention was made that animal cell culture typically have low production rates compared with bacterial cultures. See Applicant's Admissions on page 1, lines 15-18, of the specification. Additionally, an antibody produced from the method of claim 11 would be expected to be identical to the claimed antibodies since it is also an anti-CTLA4 mAB. "The patentability of a product does not depend upon its method of production. If the product in [a] product-by-process claim is the same as or obvious from a product of the prior art, [then] the claim is unpatentable even though the prior [art] product was made by a different process." *In re Thorpe*, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted). Once the examiner provides a rationale tending to show that the claimed product appears to be the same or similar to that of the prior art, although produced by a different process, the burden shifts to applicant to come forward with evidence establishing an unobvious difference between the claimed product and the prior art product. *In re Marosi*, 218 USPQ 289, 292 (Fed. Cir. 1983). In product-by-process claims, "once a product appearing to be

substantially identical is found and a 35 U.S.C. 102/103 rejection [is] made, the burden shifts to the applicant to show an unobvious difference." MPEP 2113. This rejection under 35 U.S.C. 102/103 is proper because the "patentability of a product does not depend on its method of production." *In re Thorpe*, 227 USPQ 964, 966 (Fed. Cir. 1985). The term "pharmaceutical composition for the treatment of cancer" (claim 14) is an intended use only. A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. A "pharmaceutically acceptable carrier" reads on water and therefore would be inherent in the preparation of the monoclonal antibodies.

3. Correspondence regarding this application should be directed to Group Art Unit 1645. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Remsen. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Group 1645 Fax number is 571-273-8300 which is able to receive transmissions 24 hours/day, 7 days/week.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer E. Graser whose telephone number is (571) 272-0858. The examiner can normally be reached on Monday-Thursday from 7:30 AM-6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell, can be reached on (571) 272-0974.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-0500.


10/26/08
Jennifer Graser
Primary Examiner
Art Unit 1645